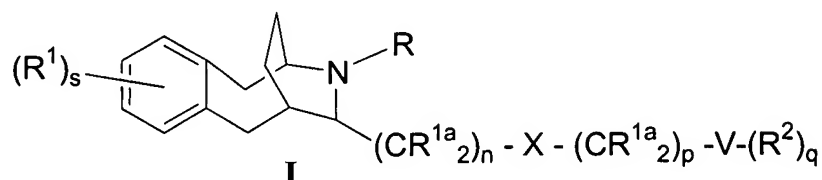


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended) A compound of Formula I



wherein

R is selected from

- 1) H,
- 2) ~~unsubstituted or substituted C₁-C₁₀ alkyl,~~
- 3) ~~unsubstituted or substituted aryl,~~
- 4) ~~unsubstituted or substituted heterocycle,~~

R^{1a} is independently selected from

- 1) H,
- 2) ~~unsubstituted or substituted C₁-C₆ alkyl, and~~
- 3) OR⁴;

R^{1b} is independently selected from

- 1) H, and
- 2) ~~unsubstituted or substituted C₁-C₆ alkyl;~~

X is selected from

- 1) a bond,
- 2) C(O), and
- 3) O,

R¹ is independently selected from

- 1) H,
- 2) halo,

- 3) OR^4 ,
- 4) NO_2 ,
- 5) ~~unsubstituted or substituted~~ $\text{C}_1\text{-C}_{10}$ alkyl,
- 6) $-\text{C}(\text{O})\text{R}^4$,
- 7) $\text{C}(\text{O})\text{OR}^4$,
- 8) $\text{C}(\text{O})\text{N}(\text{R}^4)_2$,
- 9) $\text{N}(\text{R}^4)_2$;

V is selected from aryl, ~~and heterocycle~~ benzofuran, benzodioxo and oxazolo;

R^2 is independently selected from

- 1) H,
- 2) ~~unsubstituted or substituted~~ $\text{C}_1\text{-C}_{10}$ alkyl,
- 3) $-(\text{CR}^1\text{b})_t\text{OR}^4$,
- 4) Halo,
- 5) CN,
- 6) NO_2 ,
- 7) CF_3 ,
- 8) $-(\text{CR}^1\text{b})_t\text{N}(\text{R}^4)_2$,
- 9) $-\text{C}(\text{O})\text{OR}^4$,
- 10) $-\text{C}(\text{O})\text{R}^4$,
- 11) $-(\text{CR}^1\text{b})_t\text{NR}^4(\text{CR}^1\text{b})_t\text{R}^5$,
- 12) $-(\text{CR}^1\text{b})_t\text{S}(\text{O})_m\text{NR}^4$,
- 13) $-\text{C}(\text{O})\text{OR}^4\text{R}^5$,
- 14) $-\text{NR}^4\text{C}(\text{O})\text{R}^4$,

R^4 is independently selected from

- 1) H,
- 2) ~~unsubstituted or substituted~~ $\text{C}_1\text{-C}_{10}$ alkyl,
- 3) ~~unsubstituted or substituted~~ $\text{C}_3\text{-C}_{10}$ cycloalkyl,
- 4) ~~unsubstituted or substituted~~ aryl,
- 5) ~~unsubstituted or substituted~~ heterocycle, and
- 6) CF_3 ;

R^5 is independently selected from

- 1) ~~unsubstituted or substituted~~ aryl, and
- 2) ~~unsubstituted or substituted~~ heterocycle;

m is independently 0, 1 or 2;

n is 0 to 4;

p is 0 to 4;

q is 0 1 to 4, ~~provided that when V is H or CF₃, q is 0;~~ and

s is 0 to 16; and

t is independently 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. (Currently Amended) The compound according to Claim 1 wherein R, R^{1b}, R⁴, R⁵, V and variables m, n, p, q and t are as defined in Claim 1 and

~~R is selected from~~

- 1) ~~H, and~~
- 2) ~~unsubstituted or substituted C₁-C₁₀ alkyl, and~~

R^{1a} is independently selected from

- 1) H, and
- 2) ~~unsubstituted or substituted C₁-C₆ alkyl;~~

X is selected from

- 1) a bond, and
- 2) C(O);

R¹ is independently selected from

- 1) H,
- 2) halo,
- 3) OR⁴,
- 4) N(R⁴)₂,
- 5) NO₂, and

~~V is selected from aryl and heterocycle;~~

- 1) ~~—H;~~
- 2) ~~—CF₃;~~
- 3) ~~—aryl, and~~
- 4) ~~—heterocycle;~~

R² is independently selected from

- 1) H,
- 2) ~~unsubstituted or substituted~~ C₁-C₁₀ alkyl, and
- 3) Halo,

s is 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

3. (Currently Amended) The compound according to Claim 1 wherein R, R^{1b}, X, R¹, R², R⁴, R⁵ and variables m and t are as defined above and:

R^{1a} is independently selected from

- 1) H, and
- 2) ~~unsubstituted or substituted~~ C₁-C₆ alkyl;

V is phenyl;

n is 0 or 1;

p is 0 to 3;

q is 0 1 to 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

4. (Original) A compound that is:

(6*R*,9*S*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)
benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-
(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-
(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-
(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-4-amine;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-4-amine;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-4-amine;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-4-amine;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-1-amine;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-1-amine;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-1-amine;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene-1-amine;

(6*S*,9*R*,11*S*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*S*,11*S*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*S*,11*R*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

or a pharmaceutically acceptable salt or stereoisomer thereof.

5. (Original) A compound according to Claim 4 that is:

(6*R*,9*S*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

or a pharmaceutically acceptable salt or stereoisomer thereof.

6. (Canceled)

7. (Withdrawn) A method of modulating the catalytic activity of protein kinases in a mammal in need thereof comprising contacting the protein kinase with a compound of Claim 1.

8. (Withdrawn) The method of Claim 7 wherein the protein kinase is an RTK.

9. (Withdrawn) The method of Claim 8, wherein the RTK is selected from IR, IGF-1R and IRR.

10. (Withdrawn) A method of treating or preventing a PK-related disorder in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

11. (Withdrawn) A method of Claim 10, wherein the PK-related disorder is an IGF-1R-related disorder selected from:

- 1) cancer,
- 2) diabetes,
- 3) an autoimmune disorder,
- 4) a hyperproliferation disorder,
- 5) aging,
- 6) acromegaly, and
- 7) Crohn's disease.

12. (Withdrawn) A method of treating cancer in a mammal in need of such treatment comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

13. (Withdrawn) A method of treating retinal vascularization comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

14. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a second compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) retinoid receptor modulator,
- 4) a cytotoxic agent,
- 5) an antiproliferative agent,
- 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,
- 9) a reverse transcriptase inhibitor, and
- 10) an angiogenesis inhibitor.

15. (Withdrawn) The method of Claim 14, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

16. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

17. (Withdrawn) The method of Claim 16 wherein radiation therapy is also administered.

18. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

19. (Withdrawn) A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.

20. (Withdrawn) The method of Claim 19 wherein the GPIIb/IIIa antagonist is tirofiban.

21. (Withdrawn) A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.

22. (New) A pharmaceutical composition which is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.